A A-30 **A**-30 **A A C**-40 **C**-40 **G A**-40 **G**-40 **G**-40 **G**-10

AUAAACUAAGGAAUaucuaug . uaauauau CAA

SEQ. I.D. NO. 345

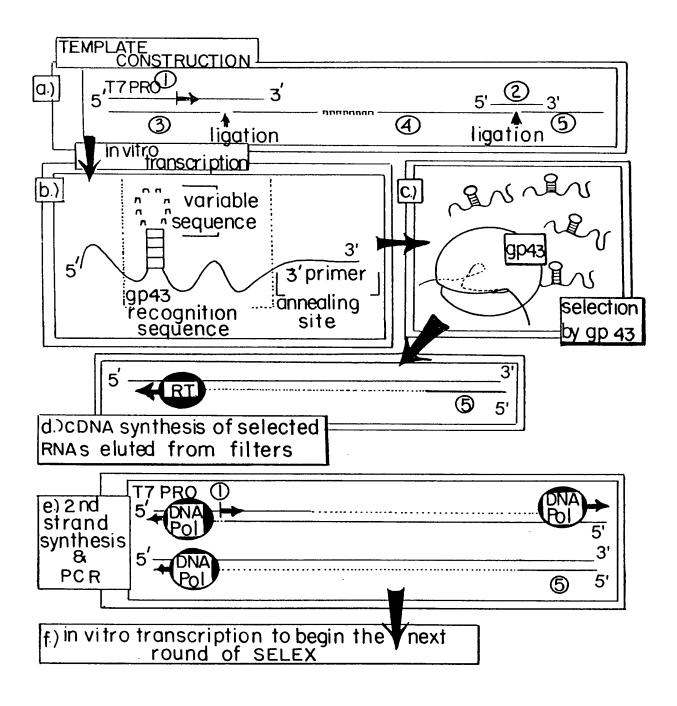


FIG.2

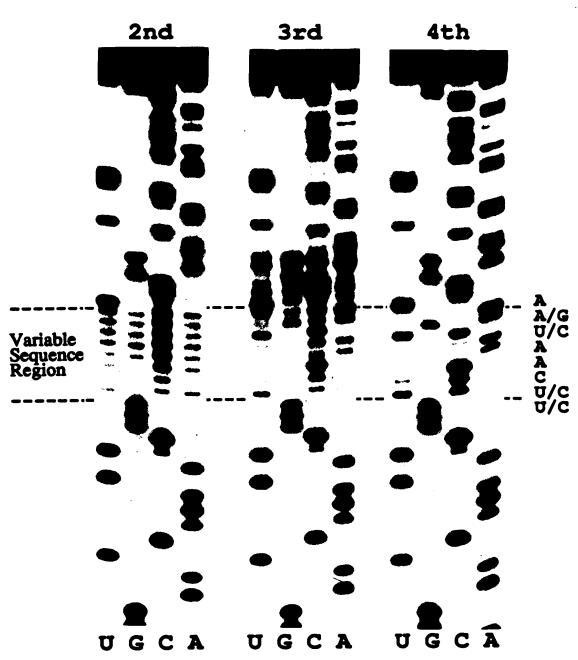
Attorney Docket No. NEX 01/C8 Sheet 3/34

Title: NUCLEIC ACID LIGANDS
Inventor: Gold et al.

Express Mail No. EL652339952US

FIG.3

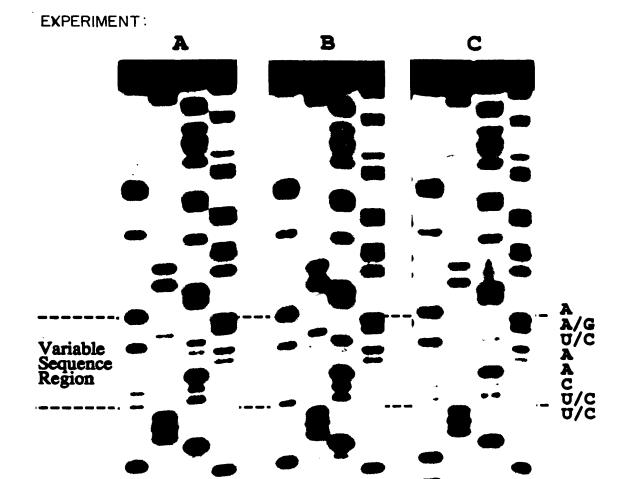
SELECTION CYCLE:



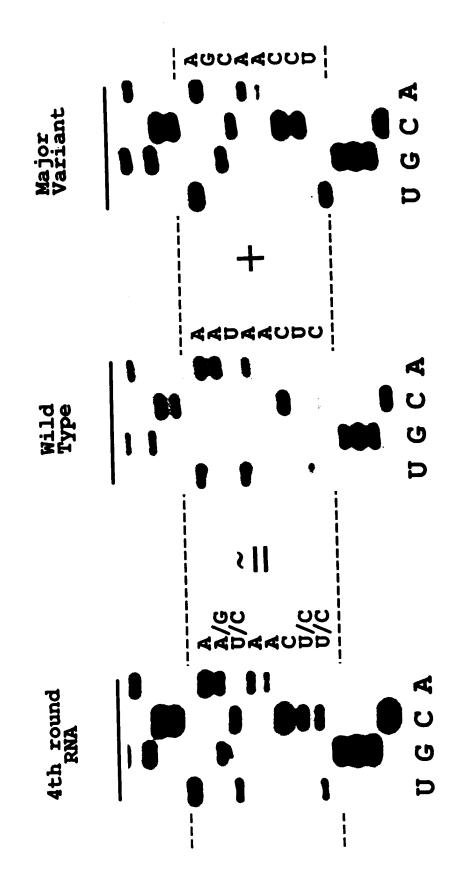
Attorney Docket No. NEX 01/C8 S
Title: NUCLEIC ACID LIGANDS
Inventor: Gold et al. Sheet 4/34

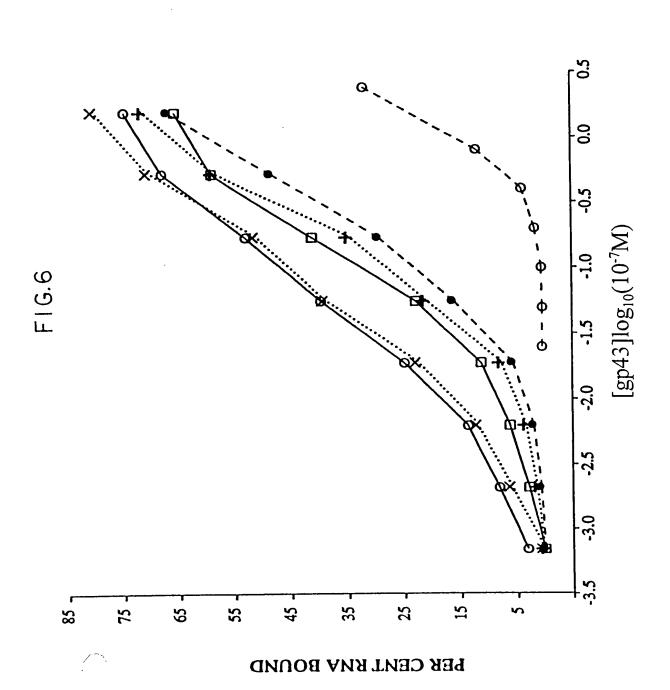
Express Mail No. EL652339952US

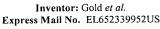
FIG.4

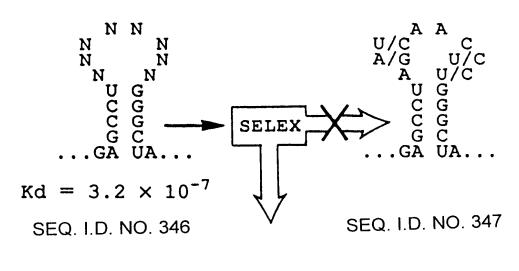


UGCA









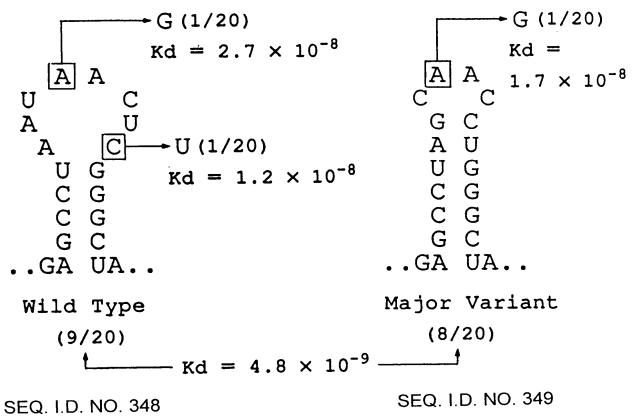
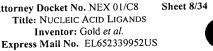
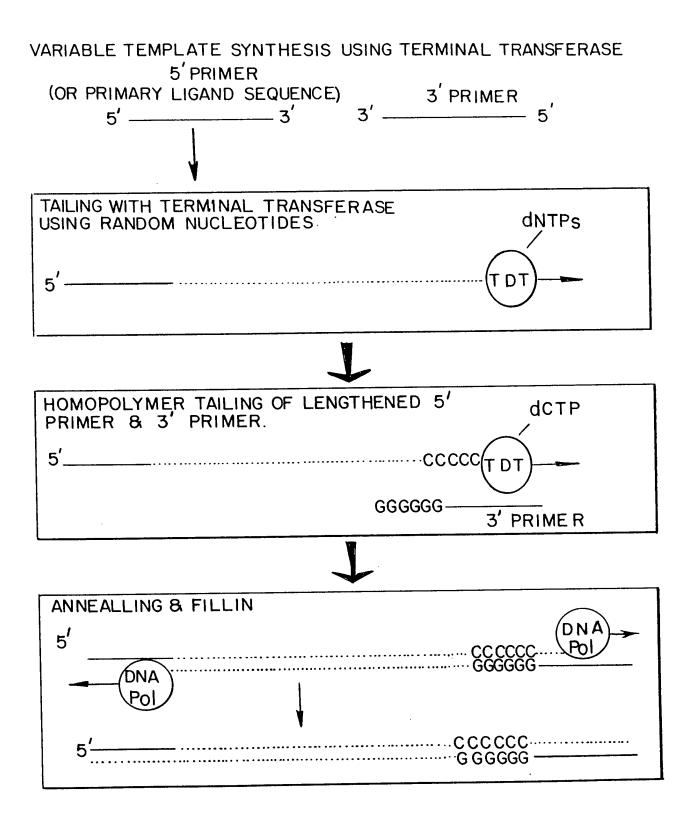


FIG.7

Attorney Docket No. NEX 01/C8 Title: NUCLEIC ACID LIGANDS Inventor: Gold et al.





"WALKING" BY EXTENDING THE PRIMARY LIGAND. **SECONDARY** ASYMMETRIC PCR

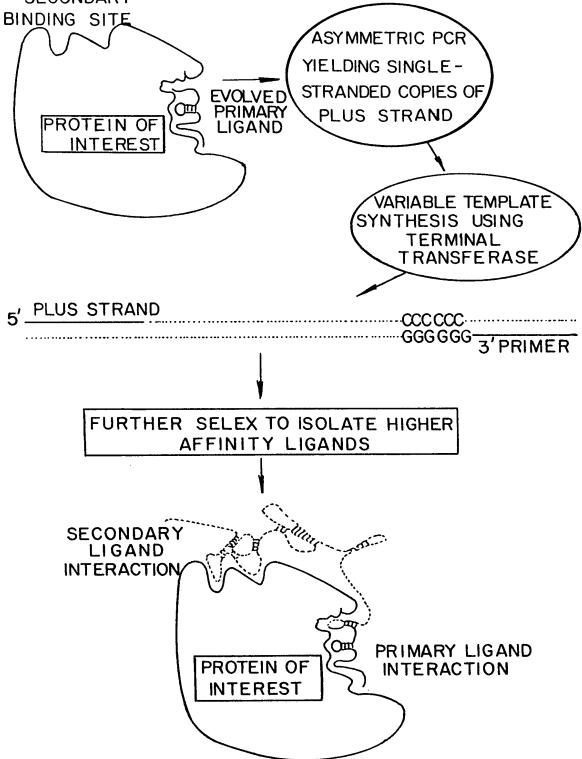
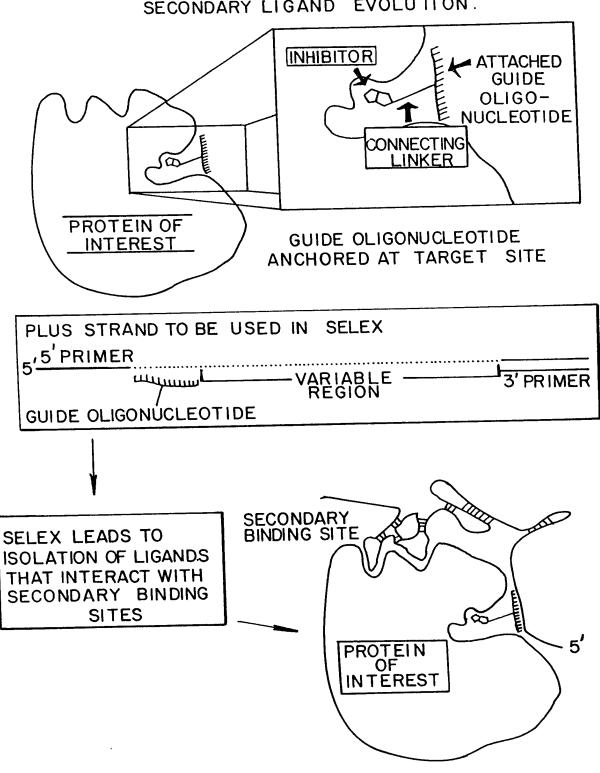


FIG.9

ANCHORING OF BRIDGING OLIGONUCLEOTIDE & SECONDARY LIGAND EVOLUTION.



F1G.10

IDDE/986 IDIBOI

SECONDARY LIGAND-DIRECTED PRIMARY LIGAND EVOLUTION .

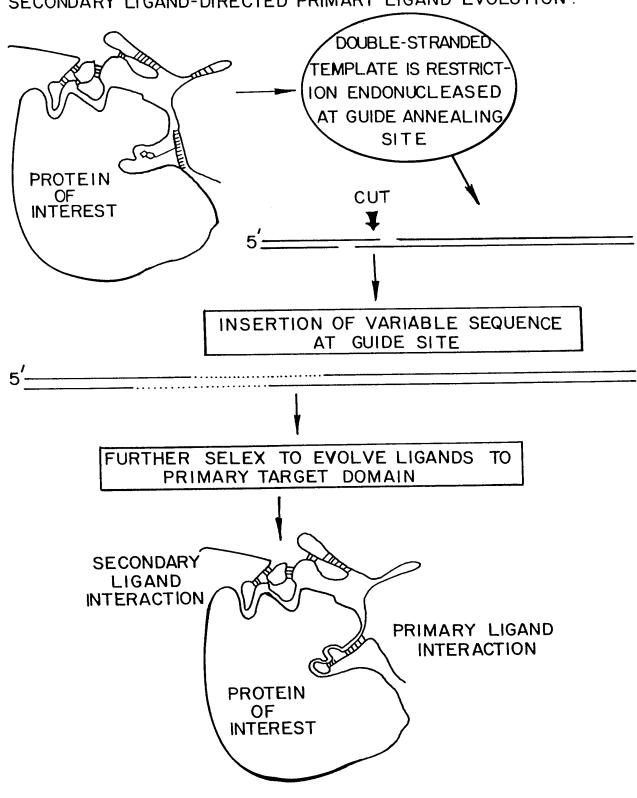


FIG.11

Express Mail No. EL652339952US

Sheet 12/34

F16.12B

5'-taatacgactcactatagggagcatcagacttttaatctgacaatcaag-. 3'-attatgctgagtgatatccctcgtagtctgaaaattagact-5'

SEQ. I.D. NO. 350

promoter

L1

SEQ. I.D. NO. 351

ligation

3'-gttagttc

in vitro transcript

-gggagcaucagacuuuuaaucugacaaucaag[32n]aucuaugaaagaauu 2,

FIG. 12 B

F16.12A

IDDS/985 "IDSED1

5'-atctatgaaagaattttatatctc-3'

3'-cttaaaatatagagataactttgcctaggcc-5'

ligation

SEQ. I.D. NO. 352

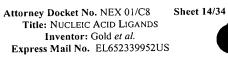
32n..tagatacttt-5'

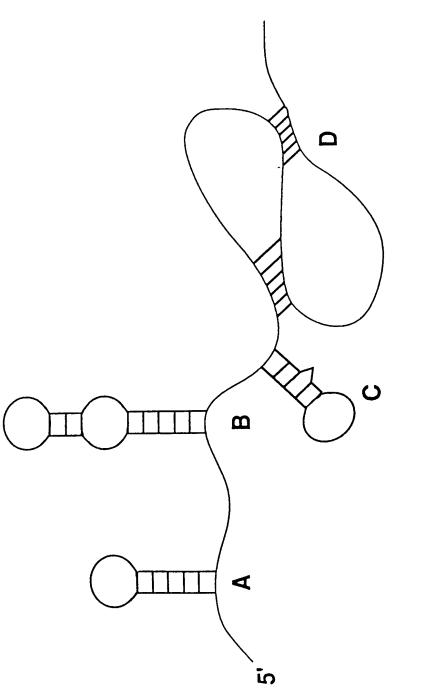
SEQ. I.D. NO. 353

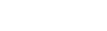
unauaucucuauugaaacggauccgg-3'

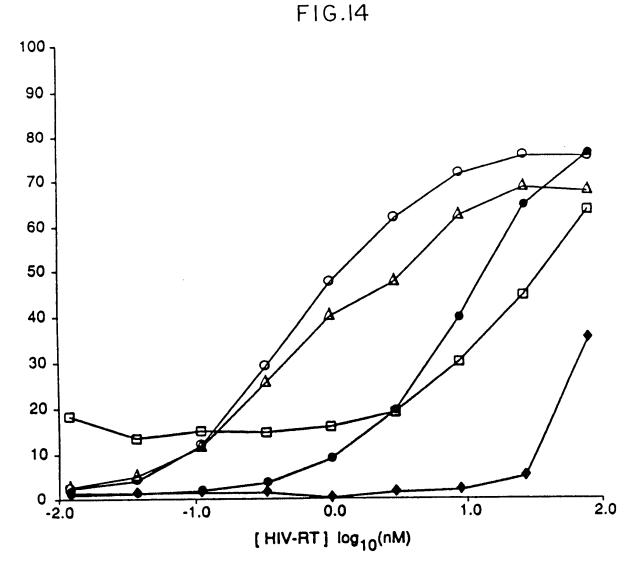
SEQ. I.D. NO. 354

F16.12B











- O 1.3 UCAGAAUAUCUUCCGAAGCCGAACCGGAAAACCGGCAUCU (1)
- 1.3 ----- A---- (1)
- ☐ 1.4 ucaagggcAUCUGGGAGGGUAAGGGUAAGGUUGUCGGaucu (4)

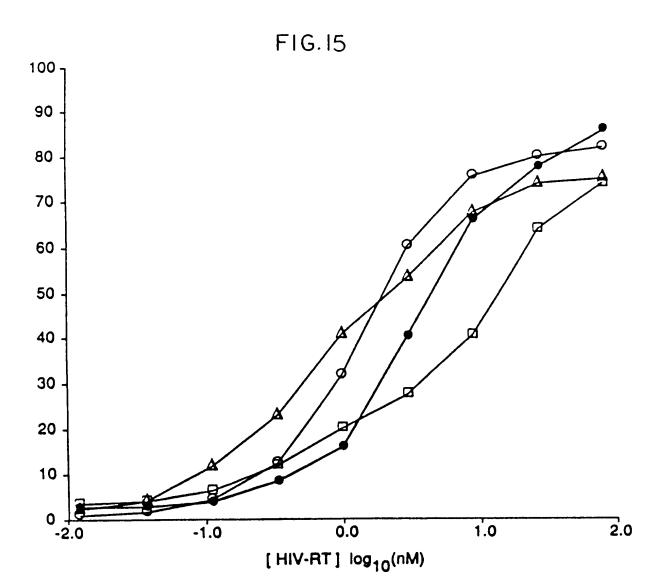
 \triangle 1.1 = SEQ. I.D. NO. 355

● 1.3 = SEQ. I.D. NO. 357

○ 1.3 = SEQ. I.D. NO. 356

☐ 1.4 = SEQ. I.D. NO. 358





O 2.1ª ucaag—AAUAUA-UCCGAACÜCGACGGGAUAACGÁGAA-Gaucu (3)

□ 2.2 b ucaaguaccuaggugauaaaagggagaacácguguga-cu (13)

• 2.5 b ucaagacaguauccguucuugaücaucaucgagacaaaúgáúcú (3)

Δ I.I ucaagAAŪUCCGUUÙÙCÀGUCGGGAAAAÁCUGAACAAUcu (I3)

O 2.1a = SEQ. I.D. NO. 359

● 2.5b = SEQ. I.D. NO. 361

 \Box 2.2b = SEQ. I.D. NO. 360

 \triangle 1.1 = SEQ. I.D. NO. 362

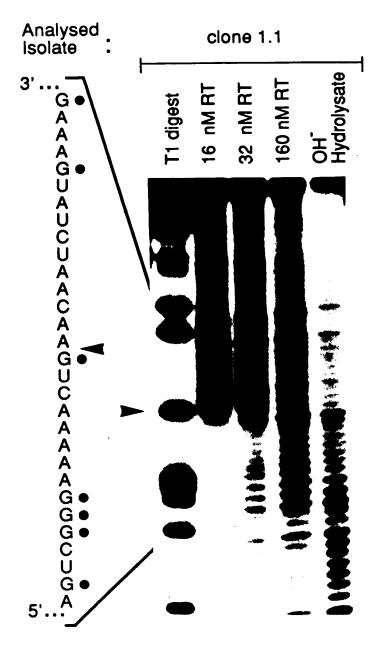


FIG. 16 A

SEQ. I.D. NO. 363

Attorney Docket No. NEX 01/C8 Sheet 18/34
Title: NUCLEIC ACID LIGANDS
Inventor: Gold et al.
Express Mail No. EL652339952US

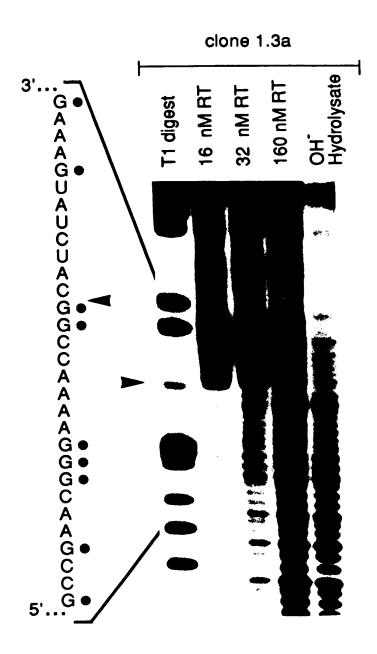
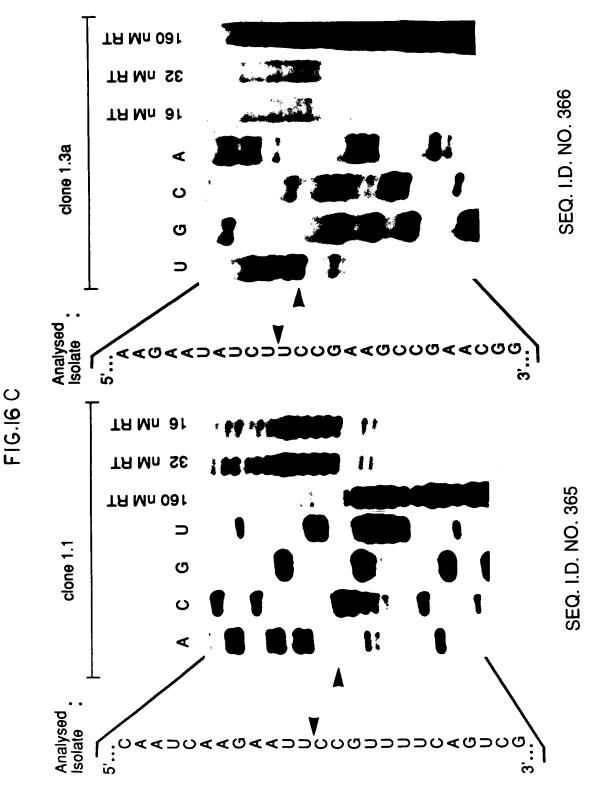


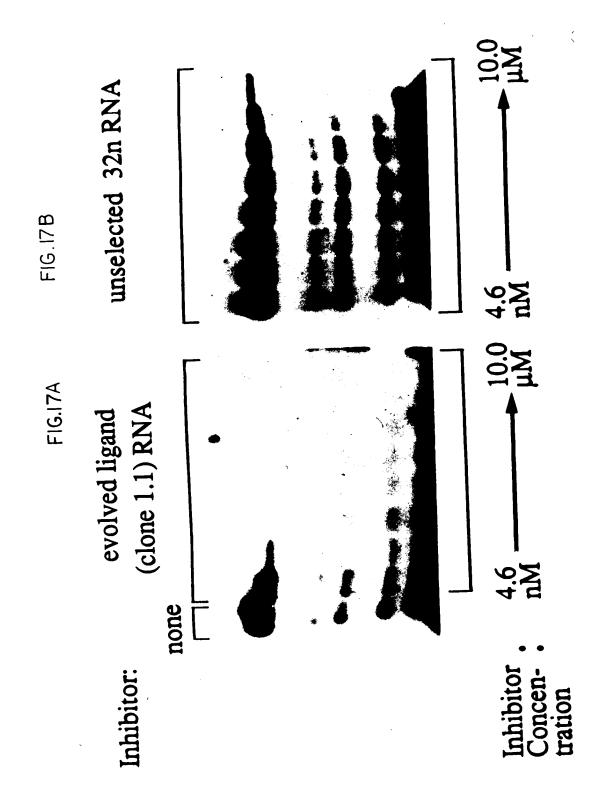
FIG.16B

SEQ. I.D. NO. 364

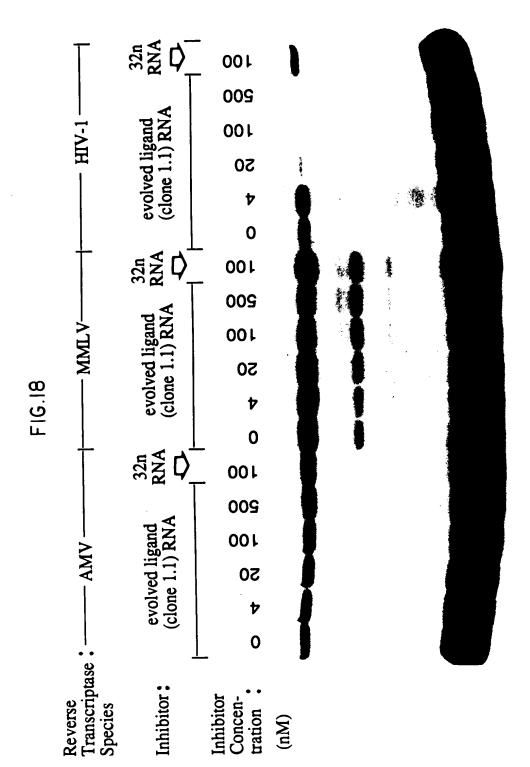


- :

Attorney Docket No. NEX 01/C8 Sheet 20/34
Title: NUCLEIC ACID LIGANDS
Inventor: Gold et al.
Express Mail No. EL652339952US

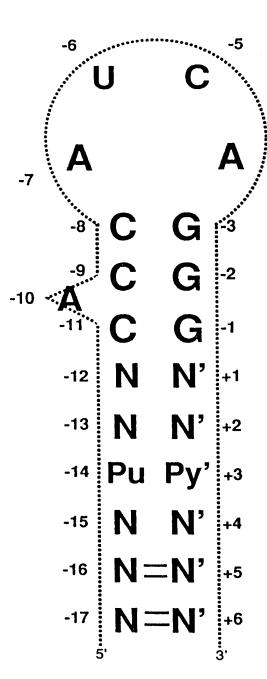


Attorney Docket No. NEX 01/C8 Sheet 21/34
Title: NUCLEIC ACID LIGANDS
Inventor: Gold et al.
Express Mail No. EL652339952US



Express Mail No. EL652339952US

FIG.19B



	Α	С	G	U	
-4	36	0	0	0	
-5	0	36	0	0	
-6	4	3	1	28	
-7	36	0	0	0	
-10	36	0	0	0	

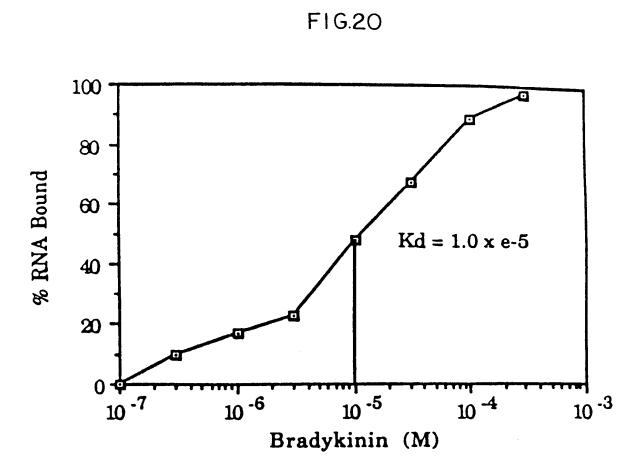
	AU	CG	UA	GC	UG	GU	Bulge	END
-8/-3	0	24	0	12	0	0	0	0
-9/-2	0	25	0	10	1	0		0
-11/-1	0	24	2	10	0	0	36	
-12/+1	8	1	8	10	7	1	0	1
-13/+2	6	5	8	9	3	1	3	3
-14/+3	9		4	10	2	3	3	4
	-	0	 	 	 	 	6	8
-15/+4	4	0	9	6	0	1	0	2
-16/+5	10	1	2	1	1	3	1	1
-17/+6	0	4	6	1	4	2		

FIG.19C

FIG.19A

SEQ. I.D. NO. 367

Attorney Docket No. NEX 01/C8 Sheet 23/34
Title: NUCLEIC ACID LIGANDS
Inventor: Gold et al.
Express Mail No. EL652339952US



Attorney Docket No. NEX 01/C8
Title: NUCLEIC ACID LIGANDS
Inventor: Gold et al.
Express Mail No. EL652339952US Sheet 24/34

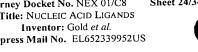
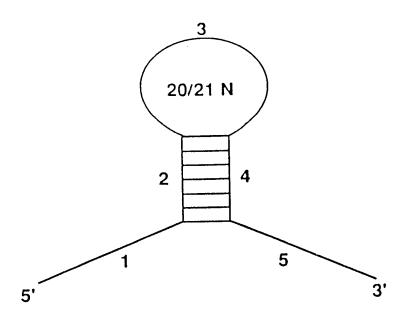
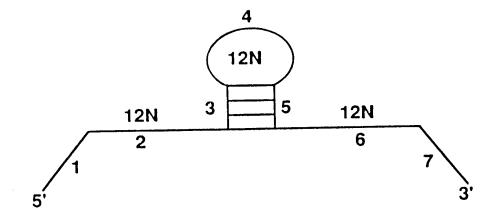
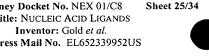


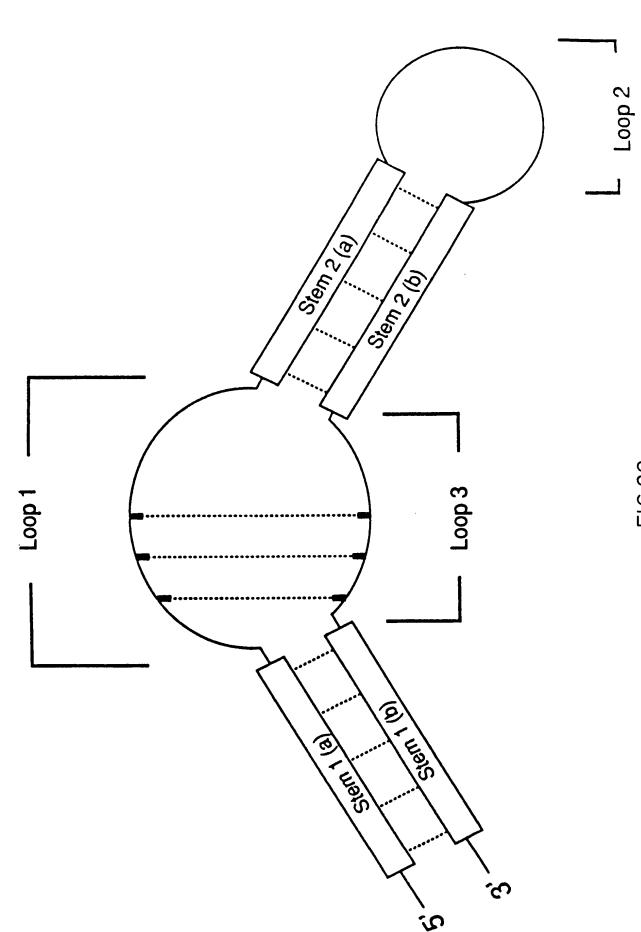
FIG.21A





F1G.21B





K

CAGC

5'...AGAUG
3'...ucuAC

-ACA-G

UCU

AAGAUA

Sheet 26/34

UUGAGAAA

Motif I (6a)

CAC U (NUCLEOTIDES 2-38 OF SEQ. I.D. NO. 301) GUG U 5'...gGGUGCA3'...ucuaUGU

Motif III (9a)

Motif II (1c)

ugaa-3' GCUU-5' CC UUGaucua-A GG SEQ. I.D. NO. 368

WT (Motif II-like Domain)

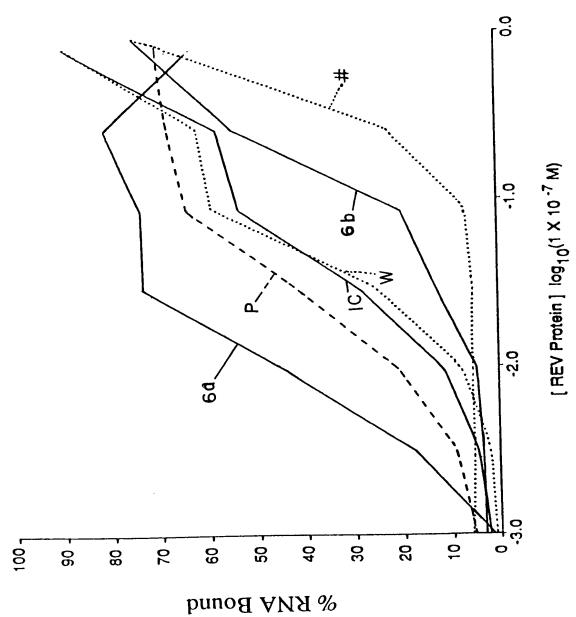
SEQ. I.D. NO. 369

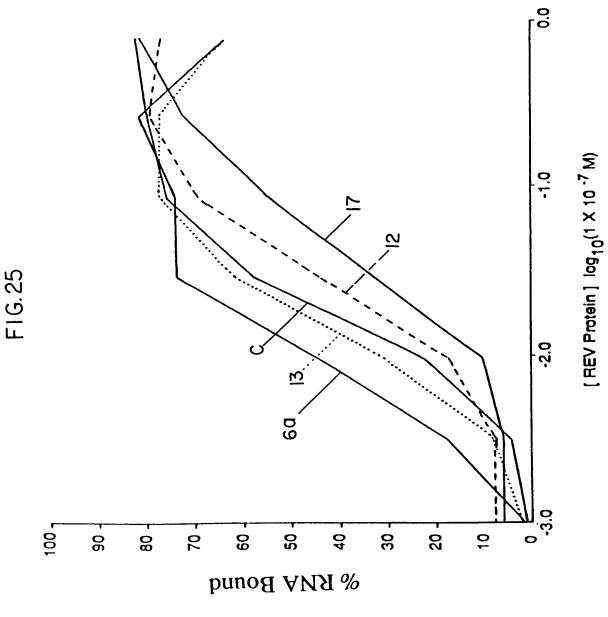
U ACGGUA
A GACGCUG || CA...
CUGCGAC || GU...

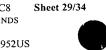
SEQ. I.D. NO. 370

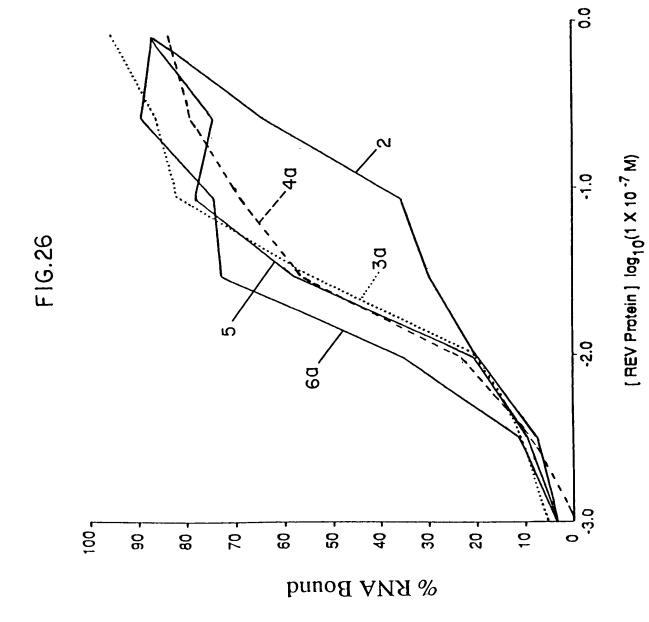
F1G. 23

HODWYGGG . HOHELE



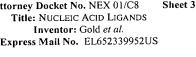


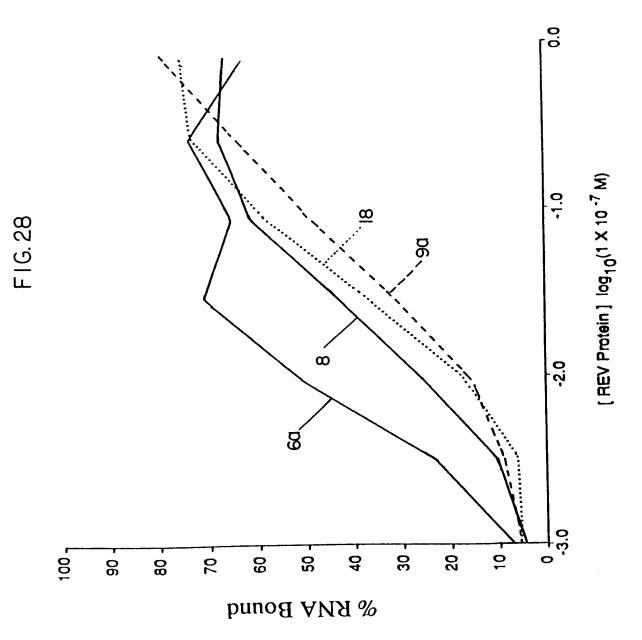




[REV Protein] $\log_{10}(1 \times 10^{-7} \text{ M})$ 50

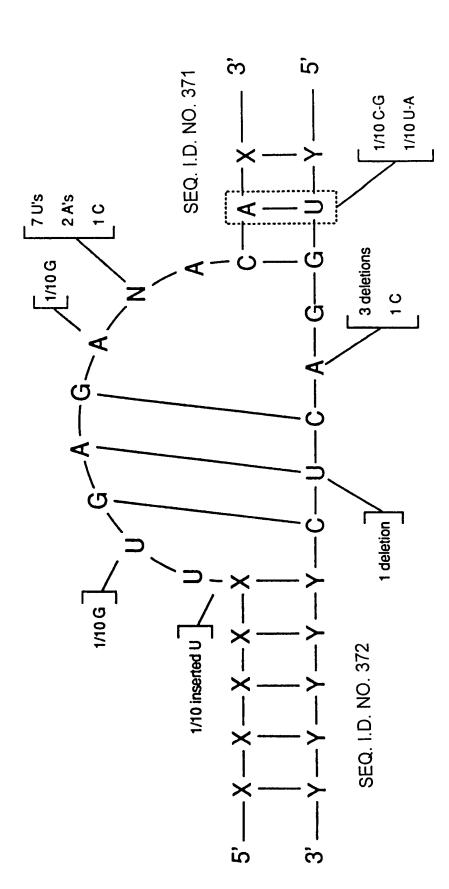
9 0 | 66 30 20 1001 6 9 5 ည 90 8 8 % KNY Bonuq

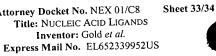


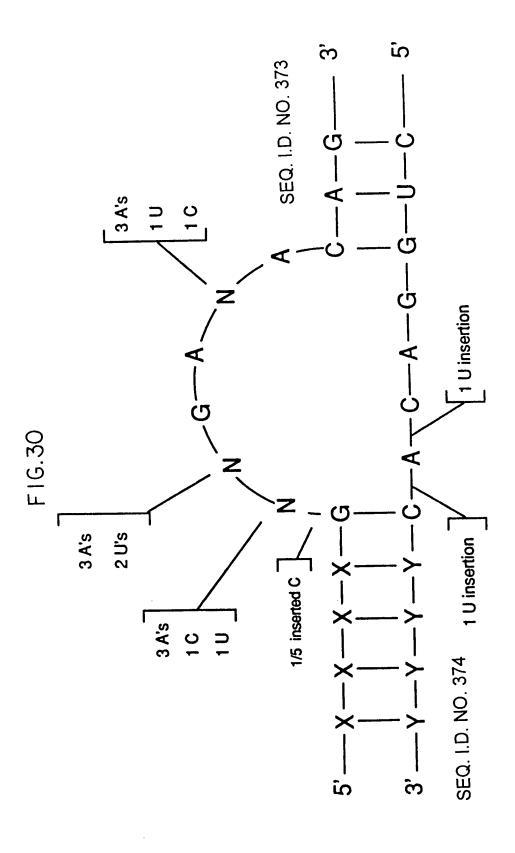




TOOTY SEG. TOILEDI







11. * #



